

## REMARKS

Claims 1, 3-6, and 8-10 constitute the pending claims in the present application. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Rejection under 35 U.S.C. 112, first paragraph. Claims 1-6 and 8-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not provide enablement for R19 and R20 together with the atom to which they are attached, forming an optionally substituted heterocyclyl ring as defined above which optionally contains further heteroatoms.

The Office Action states that there are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is “undue”. The Examiner sites the second Wands factor, wherein the nature of the invention is that these compounds are anti-inflammatory agents. The Examiner further states that the level of predictability in the art of these compounds is low, since none of these compounds are tested for their effects on the inhibition of monocyte chemoattractant protein-1 and/or RANTES induced chemotaxis. Applicants disagree and assert that the nature of the invention is the discovery that a range of highly functionalized R<sup>3</sup> substituents are possible without loss of activity. The specification exemplifies a wide range of indoles with such groups that are therapeutically active. Applicants note that this is not the first case where indoles have been found to be active in MCP-1 inhibition. Specifically, Applicants refer the Examiner to page 1, line 24 of the specification which sites PCT/GB98/02340 and PCT/GB98/02341, wherein both applications describe and claim groups of compounds based upon the indole ring structure which are inhibitors of MCP-1. As a result, Applicants submit that the predictability of activity amongst the compounds of the pending claims is higher than normal since a person of skill in the art would look to the prior art and consider that substituents present in other active compounds could be included as substituents on compounds recited in the pending claims. Applicants therefore assert that the present scope of the claims is entirely consistent with the nature of the invention. Nevertheless, solely to expedite prosecution, Applicants have amended the claims such that the definition of R4 no longer includes R19 and R20; accordingly Applicants submit that the rejection is moot. Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection under 35 U.S.C. 112, first paragraph. Claim 10 is rejected under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement. The Office Action states that the Applicant does not describe how a group R3' can be changed to a group R3. Applicants have amended claim 10 such that R3' is R3 as defined as in claim 1, therefore Applicants submit that the rejection is moot. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection under 35 U.S.C. 112, first paragraph. Claims 1 and 4-6 are rejected under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement. The Office Action states that the Applicant does not describe how an inflammatory disease is actually being mediated by monocyte chemoattractant protein-1 and/or RANTES-induced chemotaxis. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Applicants have amended the claims to replace the term "A method for treating inflammatory disease mediated by monocyte chemoattractant protein-1 and/or RANTES-induced chemotaxis" with the term "A method for treating inflammatory disease, comprising inhibiting monocyte chemoattractant protein-1 and/or RANTES-induced chemotaxis". Applicants submit that the claims as amended fully comply with the requirements of 35 U.S.C. 112, first paragraph. Furthermore, Applicants respectfully refer the Examiner to page 1, line 9 of the specification wherein "MCP-1 has been implicated in the pathophysiology of a large number of inflammatory diseases" (see WO 94/09128). Similarly, Applicants refer the Examiner to page 3, line 23 of the specification, wherein "RANTES is another chemokine from the same family as MCP-1, with a similar biological profile, but acting through the CCR1 receptor. As a result, these compounds can be used to treat disease mediated by these agents". Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

### **CONCLUSION**


In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same

and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945.**

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Respectfully Submitted,



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